Transcutaneous Electrical Nerve Stimulation for Pain Relief during Photodynamic Therapy of Actinic Keratoses

Christina B. Halldin¹, John Paoli¹, Carin Sandberg¹, Marica B. Ericson^{1,2} and Ann-Marie Wennberg¹

¹Department of Dermatology, Sahlgrenska University Hospital, and ²Department of Physics, Göteborg University, SE-413 45 Göteborg, Sweden. E-mail: christina.halldin@ygregion.se Accepted December 3, 2007.

Sir.

Topical photodynamic therapy (PDT) is an effective treatment for actinic keratoses (AKs) on the face and scalp (1, 2). The major side-effect of PDT is pain during treatment (3). Patients receiving PDT for AKs on the face and scalp often experience severe pain during treatment. The difficulty of finding a pain-relieving strategy has been highlighted in earlier studies (4, 5). Untreated AK lesions may increase the risk of developing squamous cell carcinoma (SCC) (6). Since PDT can be used to treat field cancerization, has good cure rates and gives excellent cosmetic results (7), it is necessary to find new strategies to reduce the pain experienced to an acceptable level.

Transcutaneous electrical nerve stimulation (TENS) is used as pain relief in acute and chronic pain (8). The mechanism behind TENS is based on the gate control theory (9, 10). A TENS unit consists of an external stimulator and electrodes applied directly to the skin. TENS has been investigated to treat different kinds of pain, e.g. procedural pain, with varying results (11, 12). The aim of this pilot study was to investigate whether TENS can reduce the amount of pain experienced by patients undergoing PDT of AKs located on the face and scalp.

PATIENTS AND METHODS

The study was approved by the regional ethics review board and conducted at the Department of Dermatology at Sahlgrenska University Hospital in Göteborg, Sweden. Fourteen male patients (mean age 75 years, range 46–86 years) with AKs on the face and scalp and experience of a high degree of pain during earlier PDT sessions were included. The treated area was prepared according to hospital routines using a 160 mg/g methyl aminolaevulinate (MAL) cream (Metvix, Photocure ASA, Oslo, Norway) applied for 3 h. The irradiation was performed using an Aktilite lamp (Photocure ASA, Norway) at a fluence rate of 80–90 mW/cm², and a total light dose of 37–45 J/cm². Spraying of cold water is part of the clinical routine and was therefore allowed if required by the patient.

The TENS electrodes were placed on the shoulders to avoid contact with the PDT area. This location is the nearest dermatome from the PDT area according to the manufacturer's guidelines. A high-frequency modulated pulse rate of 80 Hz was used (Cefar Primo, Cefar Medical AB, Malmö, Sweden).

The pain was assessed using a visual analogue scale (VAS). The average VAS value from previous treatments (VAS 8.1 range 6–10), served as control for each patient. This could be done since VAS assessment of the pain during PDT is performed as part of the clinical routine. The time between further PDT treatments and PDT with TENS was, on average, 14 months (range 3–31 months). In addition, a short questionnaire was

answered after completion of PDT with TENS and at the follow-up visit after 2 months.

The differences between baseline VAS scores and assessment obtained during PDT with TENS were analysed using a paired t-test (Microsoft Excel, Microsoft, USA). Error limits reported represent standard error of mean (SEM). Statistical significance was taken as p < 0.05.

RESULTS

Fig. 1 presents the difference in the VAS scores obtained at baseline (PDT without TENS) and during PDT with TENS for each patient. All but one patient with baseline VAS above 8 perceived less pain using TENS, while the 5 patients with VAS values below 8 at baseline showed a varying effect. Four patients had no effect of TENS as pain relief during PDT. Three of these patients were treated for AKs on the face and one for AKs on the scalp. Three of 14 patients (21%), had earlier interrupted PDT due to unbearable pain, but were all able to complete the treatment when TENS was used. The observed mean VAS score (± SEM) using TENS in connection with PDT was 6.2 (± 0.4) compared with 8.1 (\pm 0.3) obtained at baseline treatments without TENS. This difference was highly significant (p < 0.005), implying that TENS can reduce VAS scores during PDT. Moreover, the questionnaire revealed that

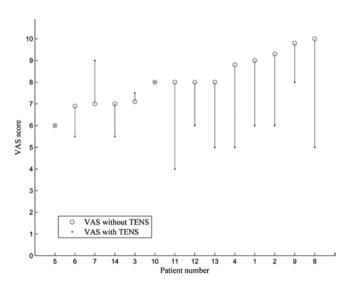


Fig. 1. Change in visual analogue scale (VAS) scores for each patient with and without transcutaneous electrical nerve stimulation (TENS) during photodynamic therapy, arranged according to the baseline value (without TENS).

the TENS procedure was easy to use and a majority of the patients (13/14) would use TENS again.

The patients with AKs on the scalp had signs of field cancerization at inclusion. All patients showed a cure rate of 80–100% after one PDT session. Remaining lesions were treated by extra PDT sessions, cryotherapy or topical 5-fluorouracil. Two patients experienced mild, easily tolerated aching of the shoulder muscles the day after the treatment, which resolved within one day. This was possibly related to the TENS procedure.

DISCUSSION

It is of great importance to find better pain-relieving strategies for patients undergoing PDT. Some patients with field cancerization in the face and scalp describe the pain experienced during PDT as equivalent to being burnt by a flat-iron. We have demonstrated that TENS reduces the VAS values during PDT when treating AKs located on the face and scalp, which normally results in high VAS scores (>8). The decrease in the average VAS score from 8.1 to 6.2 may seem minor. but it should be noted that a decrease of approximately 2 VAS points at this high level of pain enables the patients to complete the PDT session. The blocking of the nerve fibres stimulated in the treatment area might be more effective when the electrodes are placed closer to the treatment area. Hence, it is important to consider the placement of the electrodes for obtaining efficient pain relief with TENS. It is desirable further to improve the pain-relieving efficiency during PDT of AKs in these areas. Further randomized, controlled studies are needed (13). It is hoped that more specific electrode placement may improve the pain reduction using TENS during PDT.

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REFERENCES

- Braathen LR, Szeimies RM, Basset-Seguin N, Bissonnette R, Foley P, Pariser D, et al. Guidelines on the use of photodynamic therapy for nonmelanoma skin cancer: an international consensus. International Society for Photodynamic Therapy in Dermatology, 2005. J Am Acad Dermatol 2007; 56: 125–143.
- Tarstedt M, Rosdahl I, Berne B, Svanberg K, Wennberg AM. A randomized multicenter study to compare two treatment regimens of topical methyl aminolevulinate (Metvix)-PDT in actinic keratosis of the face and scalp. Acta Derm Venereol 2005; 85: 424–428.
- Sandberg C, Stenquist B, Rosdahl I, Ros AM, Synnerstad I, Karlsson M, et al. Important factors for pain during photodynamic therapy for actinic keratosis. Acta Derm Venereol 2006; 86: 404–408.
- Holmes MV, Dawe RS, Ferguson J, Ibbotson SH. A randomized, double-blind, placebo-controlled study of the efficacy of tetracaine gel (Ametop) for pain relief during topical photodynamic therapy. Br J Dermatol 2004; 150: 337–340.
- 5. Langan SM, Collins P. Randomized, double-blind, placebo-controlled prospective study of the efficacy of topical anaesthesia with a eutetic mixture of lignocaine 2.5% and prilocaine 2.5% for topical 5-aminolaevulinic acid-photodynamic therapy for extensive scalp actinic keratoses. Br J Dermatol 2006; 154: 146–149.
- Anwar J, Wrone DA, Kimyai-Asadi A, Alam M. The development of actinic keratosis into invasive squamous cell carcinoma: evidence and evolving classification schemes. Clin Dermatol 2004; 22: 189–196.
- 7. Morton CA. Realizing the cosmetic potential of topical photodynamic therapy. J Cosmet Dermatol 2002; 1: 66–71.
- 8. White PF, Li S, Chiu JW. Electroanalgesia: its role in acute and chronic pain management. Anesth Analg 2001; 92: 505–513.
- 9. Melzack R, Wall PD. Pain mechanisms: a new theory. Science 1965; 150: 971–979.
- 10. Wall PD. The gate control theory of pain mechanisms. A re-examination and re-statement. Brain 1978; 101: 1–18.
- 11. Lander J, Fowler-Kerry S. TENS for children's procedural pain. Pain 1993; 52: 209–216.
- Coyne PJ, MacMurren M, Izzo T, Kramer T. Transcutaneous electrical nerve stimulator for procedural pain associated with intravenous needlesticks. J Intraven Nurs 1995; 18: 263–267.
- Carroll D, Tramer M, McQuay H, Nye B, Moore A. Randomization is important in studies with pain outcomes: systematic review of transcutaneous electrical nerve stimulation in acute postoperative pain. Br J Anaesth 1996; 77: 798–803.